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ON THE

CAUSES AND PATHOLOGY OF PYÆMIA (SEPTÆMIA).

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REPORT ON THE CAUSES AND PATHOLOGY OF PYÆMIA (SEPTÆMIA).

THE American Medical Association, at its last annual meeting, did me the honor to appoint me chairman of a committee to report on the "Causes and Pathology of Pyæmia." This appointment was made, as I understand, at the request of my friend, Brevet Col. CHAS. S. TRIPLER, Surgeon U. S. Army, and was not known to me until after the Association had adjourned. It was the more unexpected, as for several years my best efforts have been directed quite away from the domain of surgery, to which the subject assigned is generally supposed to belong. Nevertheless, the same disordered condition of the system which modern surgeons indicate by the word Pyæmia occurs so frequently in connection with *disease* that it has been a topic of earnest thought with me, especially in its relations to the ulcerated colon of camp dysentery; and I have thought that perhaps its discussion from the medical point of view would not be without interest.

The affection to be considered is a peculiar constitutional condition, which may come on after wounds and operations, during puerperal convalescence, or the progress of certain diseases; which is characterized by febrile symptoms of a typhous character, and in fatal cases is frequently accompanied by multiple abscesses, by gangrenous foci, or by patches of parenchymatous congestion and degeneration, though, indeed, these local phenomena are far from being uniformly present.

The term Pyæmia, contracted from the Pyohæmia of Piorry, signifying pus blood, appears at the present moment to be no longer proper, since there is no good reason to believe that the presence of pus in the blood has anything to do with the disease. Virchow has proposed the word Ichorhæmia, which is much better. I must express my own preference for the designation Septæmia, literally putrid blood (σηπτος and αἷμα) as expressing more sharply the idea of an alteration in the circulating fluid under the influence of a

septic poison. The appellation *Pyæmia* is, however, in such general use that I shall retain it in the present paper with this preliminary protest.

I by no means propose to offer here an extensive essay on the subject. The burthen of other duties places this quite out of my power at present. I hope indeed to return to the theme at no very distant day, with the purpose of handling it more in detail. All that I shall now attempt is to bring together a few considerations in connection with the literature of the subject, to offer a brief summary of the leading explanations of the phenomena which have been propounded, and a criticism of the basis on which they rest—perhaps to venture on a few hints in further explanation—after which I shall conclude with a sketch of some of the more prominent forms of non-surgical *pyæmia*, and especially of uterine *pyæmia*, the *pyæmia* of new-born infants, *pyæmia* originating in intestinal ulcers and other lesions of the portal system, and the so-called idiopathic or spontaneous *pyæmia*. It will be convenient, however, to introduce the subject by a brief description of the chief phenomena of *pyæmia* in general, by which needless repetition will be avoided in subsequent portions of the paper.

The disease may begin abruptly with a chill followed by fever, or with rigors alternating with febrile flushes. During the late war I have noticed in wound-*pyæmia* that generally the first symptoms are malaise, with loss of appetite, restlessness at night, and pallor of the skin, sometimes verging on an icteroid condition. The patient frequently complains of a peculiar unpleasant taste in the mouth, which communicates itself to all articles of diet. After several days of this condition, rigors or chills make their appearance for the first time. Fever once established may present an intermittent or remittent form, but usually in the course of a very few days becomes continuous and typhoid in its character, with hot, dry skin, frequent, feeble pulse, mental disturbance soon amounting to low delirium or stupor, a red, dry tongue, which after a time becomes brown or coated with sordes, meteorism, diarrhoea, in short the symptoms of the fevers of the typhoid grade. Icterus more or less pronounced is a frequent accompanying phenomenon. These constitutional conditions, when dependent upon a visible local lesion, are accompanied by local phenomena of equal significance. If the point of departure be a wound, it will be found to have lost its healthy character, the formation of normal pus ceases, the lips of the wound become dry and livid, and often after ampu-

tations or gunshot injuries, sloughing or phagedæna sets in. The superficial veins leading from the wound are often swollen, hard, and tender; occasionally abscesses form in their track. Sometimes an erysipelatous condition of the integument commences at the wound and spreads with great rapidity. In many of these cases brought under my notice, during the late war, the erysipelatous blush was modified by a yellowish or brownish tinge intermixed with the deeper shades of red, and sloughing of the integument was not uncommon (erysipelas gangrenosa). In the cases which occur after parturition the lochia become at first fetid, then nearly or quite suppressed, the vagina is hot and dry, the lower portion of the abdomen tender, and the phenomena of metritis or metro-peritonitis are usually present. The progress of the affection is often complicated with symptoms attributable to the secondary abscesses or foci, such as difficulty of breathing, more or less cough, pain in the side, dulness on percussion, with rude or bronchial respiration, if the lungs have become their seat; jaundice, and pain or tenderness in the right hypochondrium, if the liver; swelling and tenderness in the articulation affected in the case of abscesses in the joints, etc.

The time after an injury at which the disease appears varies greatly with the nature of the injury. I have known pyæmia to set in months subsequent to a compound fracture of the femur. In the case of parturient women it usually begins during the first fifteen days; after venesection, dissecting wounds, and similar accidents, still earlier.

The duration of the disease may vary from a few days to several weeks, and in either case it is very apt to prove fatal. Where secondary foci can be recognized, a fatal result may almost always be anticipated; not invariably, however, as some have assumed; I have myself seen at least one case of recovery after the commencement of metastatic foci in the lungs. There is a class of cases remarkable for the intensity of the constitutional phenomena which prove fatal within forty-eight hours or a few days, and in which no secondary foci are found after death; while many mild cases occur unaccompanied by symptoms of such foci during life, presenting simply a typhoid depression of the system under the influence of a foul or phagedenic condition of the wound or injury, and terminate in recovery.

The conditions observed after death may be divided into two groups; those connected with the local morbid affection in which

the disease originated, and those existing in the blood or in distant organs. The essential part of the local affection is the condition of the veins which has been described by almost all writers since the time of Hunter under the name of phlebitis, and this again has been subdivided into two varieties, adhesive phlebitis and suppurative phlebitis. The conditions actually to be observed are as follows: The veins involved are more or less distended with blood-coagula, which may be quite red and firm like ordinary freshly-coagulated blood, or mixed with a yellowish or grayish pus-like fluid. Examination of the coagula in those cases in which this yellowish fluid is not abundant shows that it originates in the centres of the clots. If carefully examined with the microscope it will be found to consist simply of decomposing blood. Granules, often in a state of active molecular movement, altered red blood-corpuscles with a few scattered white corpuscles, are all that is to be seen. There is here no true pus; and the name of suppurative phlebitis is therefore a misnomer. Whether or no pus is ever to be found in such situations I am not prepared positively to assert. I certainly have never seen it, although I have examined a number of cases. It is to be borne in mind that the white corpuscle of the blood is not distinguishable from the pus corpuscle; and as the debris of the softened clot must contain a number of these proportioned to the amount of blood which has undergone alteration, it might readily happen that some of them seen microscopically should induce an observer to characterize the yellowish fluid in which he saw them floating as pus. This would be especially apt to be the case if he commenced the investigation expecting to find pus in the site examined. To justify the application of the name of pus to such a fluid, however, it should be shown either on the one hand that there is some distinctive mark by which the white corpuscle can be distinguished from the pus cell, or, on the other hand, that the number of corpuscles is too great to be accounted for by supposing them to belong to the altered blood. Neither of these possibilities can be proven. The two kinds of corpuscles have no anatomical distinctive marks, and in all the cases in which I have examined the pus-like fluid under consideration, the recognizable white corpuscles were so few as to compel the supposition that a large part of those belonging to the softened clot had undergone degradation into the same granular debris into which the fibrin and most of the red corpuscles had been transformed.

The credit of first showing the real nature of the pus-like fluid

in these cases, is usually assigned to Virchow, but very incorrectly. Long before the publication of his *Essays*, Gulliver, in England, had pointed out the errors which existed in the previous descriptions of suppurative phlebitis, and had arrived at the following conclusions:—

“1st. That coagulated fibrin, when removed from the body and subjected to a blood-heat, commences to soften in about forty hours, assuming the color and consistency of pus, but easily distinguishable from it by microscopic and chemical examination.

“2d. That the purulent-like fluid found in the fibrinous clots of the heart and arteries, and so frequently in the veins, is essentially distinct from pus, and analogous, if not identical, with softened fibrin.

“3d. That the softening of coagulated fibrin is an elementary pathological condition of frequent occurrence, distinct from suppuration, and constituting a considerable proportion of the cases generally denominated suppurative phlebitis.”¹

The transformation of the coagulated blood into a puriform fluid, commencing at the centre of the clot, may ultimately involve its whole substance and the vessel is then found filled with a fluid which, in its appearance, more or less closely resembles pus, but which, in its origin and microscopic characteristics, differs radically from it. Where the disease is associated with a gangrenous surface, as in certain sloughing wounds, the peculiar decomposition of the clot here described may pass into a form of putrefaction not unlike that occurring in the gangrenous part itself; and the puriform fluid in the bloodvessels is found to possess a putrid smell, and to consist of a mass of extremely minute granules in a state of active molecular movement.

The foregoing remarks will serve to indicate the basis upon which, in my opinion, the usual doctrine of suppurative phlebitis rests.

The condition described as adhesive phlebitis, is simply the stage of the process in which the clots fully formed have not yet begun to undergo degradation.

These criticisms are not to be understood as denying the possibility of a true phlebitis, which indeed may coexist with any of the stages of clot formation or degradation I have sketched. True phlebitis is characterized by a thickening of the coats of the affected

¹ “On the Softening of Coagulated Fibrin,” by George Gulliver, F. R. S., Assistant Surgeon to the Royal Regiment of Horse Guards. (*Medico-Chirurgical Transactions*, vol. xxii. p. 136. See also *London Medical Gazette*, March, 1839.)

vessel, due to multiplication of their elementary forms, sometimes even by abscess formation in the substance of the vascular walls or in the surrounding connective tissue. I am not prepared to assert positively that lymph or pus formation can, under no circumstances, occur on the inner surface of the veins; but the very class of cases relied upon to prove such "exudative processes" fail, as has been just shown, to bear analysis.

The alterations existing in the blood or in organs at a distance from the primary seat of the disease, have next to be considered. *The blood*, to which naturally attention has been earnestly directed, affords little information of significance. Observations have chiefly been directed to the question of an admixture of pus, whether proceeding from phlebitis or introduced from without by absorption or through the patulous orifices of open veins. For a long time it was supposed that this question had been settled in the affirmative. Not only was a fluid supposed to be pus found in connection with the so-called phlebitis, as has already been mentioned, but accumulations of corpuscles, believed to be pus-corpuscles, were found in the sinuses of the dura mater and elsewhere; and the presence of numerous similar corpuscles, in the blood was clearly demonstrated by many microscopical observers. Unfortunately this *pus-blood* did not always or even generally coexist with suppurative phlebitis or with any of the secondary phenomena of pyæmia; on the contrary, its most exquisite development was generally in cases in which none of the symptoms of pyæmia were observed during life and none of its pathological appearances after death. This naturally drew attention to the comparative morphology of pus and of white blood-corpuscles; and this comparison, with a careful analysis of cases, resulted in the doctrine of Lukæmia, which recognizes in these cases simply an abnormal increase of the number of the white corpuscles of the blood coincident with enlargement of the spleen or of the lymphatic glands. The credit of this doctrine undoubtedly belongs to Virchow; although it has been claimed by Bennett, whose argument in favor of his own priority seems to have been generally admitted in this country and in Great Britain. The argument by which Bennett has attained this reputation requires some comment.

In November, 1845, Virchow published in Froriep's *Neue Notizen*, under the designation, "Weisses Blut," a case in which the blood contained immense numbers of white blood-corpuscles. He not only described the corpuscles, but he recognized their nature.

"When I, therefore, speak of white blood," he says, "I mean, in fact, a blood in which the proportion between the red and colorless corpuscles is reversed, without any noticeable admixture of foreign chemical as morphological elements." In the same paper he quotes a case of so-called general pyæmia observed in Vienna,¹ of which he suggested that it is probably erroneously so-called, and is in fact a case similar to his own.

On the other hand, Bennett claims that he had published a similar case six weeks before in the *Edinburgh Medical and Surgical Journal*, for 1845, page 413, and in his "Clinical Lectures"² he gives what purports to be a "*verbatim*" reprint of the original paper. A comparison of this reprint with the original paper shows, however, not only that it does not describe an increase of the white corpuscles of the blood, the possibility of which is indeed expressly excluded from the interpretation of his case, but that it differs in several important particulars from the original paper, as may be shown by a few parallel passages:—

Original paper in the Edinburgh Medical and Surgical Journal.

"Case of hypertrophy of the spleen and liver in which death took place from suppuration of the blood."

"The yellow coagulum of the blood was composed of coagulated fibrin in filaments, intermixed with numerous pus corpuscles, which could be readily squeezed out from it when pressed between glasses."

"The red portion of the coagulum contained a large number of these pus-corpuscles mixed, however, with a multitude of normal yellow corpuscles."

"The pus-corpuscles above described were found in the blood throughout the system."

"The enlarged lumbar glands, on being pressed, exuded a fluid that was crowded with corpuscles; some resembling those of pus already alluded to; others oval, containing a distinct nucleus."

"Acetic acid produced the same changes in these as in the pus-corpuscles found in the blood."

Reprint of the same in the Clinical Medicine.

"Leucocythemia discovered after death. Hypertrophy of the spleen, liver, and lymphatic glands. Absence of phlebitis and of purulent collections in any part of the body."

"The yellow coagulum of the blood was composed of coagulated fibrin in filaments, intermixed with numerous colorless corpuscles, which could be readily squeezed out from it when pressed between glasses."

"The red portion of the coagulum contained a large number of these colorless globules, mixed, however, with a multitude of normal yellow corpuscles."

"The colorless corpuscles now described were found in the blood throughout the system."

"The enlarged lumbar glands, on being pressed, exuded a fluid crowded with corpuscles; some resembling the colorless corpuscles already alluded to, others oval and round, containing a distinct nucleus."

Omitted in the reprint.

¹ From the Zeitschrift der K. K. ges. der Aertze zu Wien, 1845; Band II. s. 488.

² Clinical Lectures on the Principles and Practice of Medicine. American edition of 1860, page 814. By John Hughes Bennett, M. D.

It will be seen, by comparing the above, that in the reprint the words colorless corpuscles are substituted for the words pus-corpuscles in four different places, which are all in which they occur in the original, except in the sentence which is omitted in the reprint, and that the title of the paper is changed. After presenting this reprint, Dr. Bennett continues as follows:¹—

“In the remarks originally appended, I observed: ‘The points connected with this case that require discussion are, 1st. The connection between the symptoms and morbid appearances; 2d. Were the corpuscles contained in the blood really those of pus? and 3d. If so, how were they produced.’ The discussion of these theoretical points, it appears to me, has nothing whatever to do with the correctness or incorrectness of the facts above detailed, which, it will be observed, are studiously separated from everything of a hypothetical character.” How studiously this separation was made may be learned not only from the frequent repetition of the words “pus-corpuscles” in the “microscopic examination,” and the heading of the case “in which death took place from suppuration of the blood,” but in such passages as the following, which I quote from the original article in the *Edinburgh Journal*. “In the present state of our knowledge, then, as regards this subject, the following case seems to me particularly valuable, as it will serve to demonstrate the existence of true pus, formed universally within the vascular system, independent of any local purulent collection from which it could be derived.” “I think there can be little doubt that pus in the blood was the cause of death, and that it produced the febrile symptoms.” “When, then, we take into consideration the existence of these corpuscles throughout the vascular system, their general size and appearance, and, above all, the changes they underwent on adding water and acetic acid, there can be little doubt that they were true pus-globules.” “But can we explain the production of pus independent of inflammation? We reply in the affirmative. The corpuscles of pus arise in the blastema formed of liquor sanguinis. This fluid, when exuded through the blood-vessels, does not thereby in itself undergo any change. If any circumstances, therefore, should arise by means of which it could be separated from the red corpuscles within the vessels, there is no reason why these pus-cells should not be formed in it.” And finally, “Positive facts, therefore, indicate that pus can form in liquor sanguinis within the vessels independent of inflammation.”

¹ Clinical Medicine, p. 819.

Such is the tenor of all the "*remarks*," and the possibility that these "pus-corpuscles" might after all be the "colorless corpuscles" of the blood is only alluded to, to be positively rejected. "With regard to the colorless corpuscles of the blood, we know of no instance where they existed in the amount, or ever presented the appearance described."

It is thus seen that Bennett's case was believed by himself to be simply one of *pus in the blood*. He himself, in his modern argument, admits nearly as much, but seems to think that the actual observation of a pus-like substance in the blood, with enlarged spleen, and without local inflammation, was, after all, *the point* of originality, and that his erroneous interpretation should not rob him of the credit of the observation. But the presence of pus in the blood played a conspicuous part in all the notions of pyæmia current at that day, and not only Craigie, as Bennett himself admits, but others, had observed precisely similar cases. Duplay,¹ for example, more than ten years previously had described a case of the presence of pus in great quantities in the arterial and venous system, without appreciable origin. In this case there was enormous enlargement of the liver and spleen. Like Bennett's, it was undoubtedly a case of leukæmia erroneously understood.

Returning after this digression, demanded by the truth of history, it is to be remarked that the failure to establish the contamination of the blood with pus in cases of pyæmia has left us without any definite information as to what alterations of this fluid are really present. Some have laid great stress upon the disposition of the blood to coagulate, and inferred thence an increase in the quantity of its fibrin, which, however, could usually be admitted only in the earlier stages of the disorder. A deficiency of fibrin has been assumed on the other hand. A condition of the corpuscles like that seen in the earlier stages of putrefaction has also been mentioned. But on none of these heads has sufficient testimony been offered to render the doctrines based upon them plausible. And the same may be said of the notion of Mackenzie,² which attributes the phenomena, in women after parturition, at least, to the accumulation of lactic acid in the blood.

¹ Observation d'une alteration très-grande du sang. Présence d'une quantité très-grande de pus dans le système artériel et veineux sans origine appréciable. Par M. A. Duplay. Archiv. Gén., II. série, t. vi. p. 223. 1834.

² Researches on the Pathology of Obstructive Phlebitis and the Nature and

Of the *secondary formations* in distant organs by far the most frequent exist in the lungs. They are sometimes true abscesses, containing ordinary pus-cells; this, however, I have only seen occasionally. Much more frequent are hard, yellowish, irregular nodules, sometimes softened in the centre into a pus-like fluid, in which the microscope detects only granules and amorphous debris of the lung tissue in various stages of granular degeneration. Associated with these yellowish nodules are often others, which present on section a reddish color with small ecchymosed spots. These exhibit on microscopical examination, an appearance similar to the yellowish, except that the normal lung elements are not so completely obliterated, and that a large number of normal or more or less altered red blood-globules are plainly observable in the scrapings from the surface of sections. The reddish nodules frequently exist in cases in which there are no yellowish ones, and often present in their centres a larger or smaller portion of yellow substance, quite like that of the yellow nodules. On the whole, it appears probable that the reddish nodules are the primary formation, that they are converted by a peculiar form of breaking down (similar to that which occurs in the blood clots, already described) into the yellowish ones, and that where true pus is found it is due to ordinary inflammation in the tissues surrounding the nodule. In view of these considerations, and especially of the frequent absence of all true pus, I prefer the term *secondary foci* to the more usual designation, metastatic abscess.

The foci in the lungs vary in size from that of a millet seed to masses of considerable bulk; their shape almost always corresponds to that of some individual lobule or group of lobules. Generally they are situated on the periphery of the organ, just below the pleura; sometimes, however, they are scattered through its substance. They are said to be more frequent in the left lung than in the right,¹ and in the lower than in the upper lobes.² Associated with them is usually a certain degree of pleurisy, with serous effusion, and the formation of a yellowish or opaque lymph, which coats the foci on the lung surface, or extends beyond them over the

Proximate Cause of Phlegmasia Dolens. By F. W. Mackenzie, M.D. (Med.-Chirurg. Trans., vol. xxxvi. p. 169.)

¹ Callender. In Holmes' System of Surgery, vol. i. p. 276. London, 1860.

² Dance. De la phlebite uterine et de la phlebite en générale. (Archiv. générales, t. xix. p. 167.)

pleura. Sometimes the pleural sac is more or less distended with pus.

The description above given of secondary foci in the lungs applies in the main to those observed in the liver, spleen, and kidneys. In all these organs there may be reddish indurations, with or without a yellowish central spot, yellowish indurations, or true abscesses; of course on microscopical examination the characters of the debris are found to vary with the organ involved. Similar foci are sometimes observed in the subcutaneous connective tissue, also in the muscles and skin, but more rarely. In the latter situation they give rise to the formation of peculiar small carbunculous foci, to a peculiar pustular eruption, or to gangrenous spots.¹ Besides foci of the character described, accumulations of true pus may take place in the ventricles of the brain, or in the joints. The larger joints are generally involved; the knee most frequently—next the shoulder. The accumulation of pus in the joints is often associated with tumefaction, and even heat and redness of the surrounding parts.

After this brief survey of the symptoms and pathological anatomy of the disease, the various attempts at its interpretation have next to occupy our attention. These efforts largely refer to the secondary foci, which, however, it must be distinctly understood, though frequent concomitants, are not essential to the existence of pyæmia.

The occurrence of multiple abscesses in the liver, lungs, and other parts of the body after injuries had long been known in medicine. Such observations had been placed on record by Massa,² Meekren,³ Pacchionius,⁴ Schmucker,⁵ Morgagni,⁶ Desault,⁷ and many others. Especially had attention been drawn to the occurrence of abscesses in the liver after injuries of the head, for which various explanations were offered. Of these the most important was that of Morgagni, who regarded them as due to the translation of pus from the seat of primary injury by means of the bloodvessels. He relates four cases of wounds of the head followed by abscesses in the

¹ Dance. *Loc. cit.*, t. xix. p. 30.

² Nicholai Massæ, *Anatomia Liber Introductorius*. Venetiis, 1559, p. 56.

³ *Observationes Medico-Chirurgical*. Amstelodami, 1682, p. 23.

⁴ *Opera*. Romæ, 1741, p. 63.

⁵ *Chirurgische Wahrnehmungen*. I. Theil, Berlin, 1774, p. 55.

⁶ *De Sedibus et Causis Morborum*, lib. iv., epist. 51.

⁷ Desault. *Jour. de Chirurgie*, t. ii. p. 11. Paris, 1791.

lungs, in one of which there were also abscesses of the liver, and quotes from Bonnet's "Sepulcretum" to show that other organs may be involved, as the spleen, the mesentery, and the heart. This doctrine of actual metastasis was generally accepted for a time; it found a supporter as late as 1832, in no less a person than Velpeau,¹ and the terms metastatic abscesses and metastatic foci derived from it are still current in medical literature. One of the circumstances which strengthened the opinion was the alleged absence of the marks of inflammation around the margin of secondary abscesses; it was hence argued that the pus found could not be of local origin. Arnott² quotes a passage from the pathological observations of Chester, published in 1766, which shows that this apparent absence of inflammation had attracted notice even at that early period. Velpeau³ particularly insists upon the doctrinal importance of this point, declaring that he had seen in these cases "abscesses around which the most attentive and minute observation did not permit the recognition of the least lesion of the organic elements."

Practical difficulties, however, arose with further investigation. More accurate observation showed on the one hand that whenever true pus was found in the secondary foci, it was formed by an inflammatory process quite like that by which pus is formed elsewhere, and on the other hand that very often the foci contain no pus, but merely granular matter, commingled with the broken down debris of the normal tissues involved. A correct knowledge of the size of the pus-corpuscles moreover demonstrated the impossibility of pus being taken up by absorption, or of its exudation into the tissues, supposing it to be introduced into the blood through the open orifices of wounded veins. These considerations would undoubtedly have ultimately overturned the doctrine of metastasis had it not earlier become obsolete through the influence of the Hunterian theory of phlebitis. The essay of John Hunter on inflammation of the veins,⁴ although containing no reference to multiple abscesses of the internal organs, was followed by other efforts in the same direction, in which the Hunterian doctrine of phlebitis was made to play a conspicuous part in the explanation of all the constitutional and anatomical phenomena of pyæmia. Prominent among

¹ Noveaux Elements de Médecine Operatoire. Paris, 1832, t. i. p. 39.

² Med.-Chir. Trans., vol. xv. p. 62.

³ Loc. cit., p. 50.

⁴ Observations on the Inflammations of the Internal Coats of the Veins. Transactions of a Society for the Improvement of Medical and Chirurgical Knowledge, vol. i. p. 18. 1793. Also Hunter's works by Palmer.

these may be mentioned the essays of Abernethy,¹ Hodgson,² Travers,³ Carmichael,⁴ Rose,⁵ and Arnott.⁶

Hunter's essay referred simply to the morbid condition which occasionally follows venesection, and he proposes two possible modes of accounting for fatal cases. "It may either be that the inflammation extends itself to the heart, or that the matter secreted from the inside of the vein passes in considerable quantity to the heart and mixes with the blood." Both Abernethy and Hodgson adopted this twofold opinion, with little modification. Travers, however, rejected both possibilities, and attributed the constitutional symptoms merely to the extent of the venous surface involved. "If we consider," he says, "the importance of the veins in the economy, the extent of the surface which the collective area of the venous tubes affords, larger, I imagine, than any of the shut sacs of the body, and the diffused and disorganizing character of the inflammation, we can surely be at no loss to account for the disturbance of the system." This suggestion, however, failed to command confidence, and after Arnott had shown that the extension of inflammation from the seat of the primary affection along the veins to the heart could not be demonstrated in the autopsy, the opinion advocated by him that the constitutional symptoms and the secondary lesions were due to the admixture of pus or other inflammatory secretions with the circulating fluid, was very generally received. Arnott's elaborate paper was not based merely on the sequelæ of wounds, but an important part of his observations referred to the so-called uterine phlebitis. The same may be said of the essay of Dance,⁷ published nearly simultaneously

¹ On the Ill Consequences sometimes succeeding Venesection. (Surgical Observations by John Abernethy, F. R. S. Philada. ed., 1811, pp. 83-104.)

² Hodgson on Diseases of the Arteries and Veins. London, 1815.

³ Surgical Essays by Astley Cooper, F. R. S., and Benjamin Travers, F. R. S. 3d edition, London, 1818, vol. i. p. 286.

⁴ Carmichael. Observations on Varix and Venous Inflammation. (Transactions of King's and Queen's College of Physicians in Ireland. Dublin, 1818, vol. ii. p. 355.)

⁵ Observations on Deposition of Pus and Lymph occurring in the Lungs and other Viscera, after Injuries of different parts of the Body. By Thomas Rose, Esq. (Med.-Chir. Trans., vol. xiv. p. 251.)

⁶ A Pathological Inquiry into the Secondary Effects of Inflammation of the Veins. By James M. Arnott. Read Oct. 1828. (Med.-Chir. Trans., vol. xv. pp. 1-131.)

⁷ Dance. De la phlébite utérine et de la phlébite en général considérées principalement sous le rapport de leurs causes et de leurs complications. (Archiv. Générales, t. xviii. p. 472, and t. xix. pp. 5 and 161.)

in Paris, which advocated similar views, and continued to be the chief French authority in this direction for the next twenty years. The subject had previously attracted the attention of several French physicians, and cases and remarks have been published by Breschet,¹ Velpeau,² Bouillaud,³ Andral,⁴ and Louis.⁵

But the precise manner in which the pus thus introduced produced its effects, and especially how the secondary foci arose, was not so easily settled. The coarser mechanical explanation of metastasis derived from the earlier observers was not readily reconciled with the fact that the foci did not always contain pus, or with the large quantity of pus sometimes found in them where the original local condition was comparatively trifling. Both Arnott and Dance simultaneously abandoned this explanation as untenable. "I think it right, however, to state," says Arnott,⁶ "that I must not be considered as regarding the matter so deposited to be actually that which has been brought into the circulation from the inflamed vein or veins." "The question is no longer one of a translation of matter merely, but one which involves the very difficult subject of the pathology of the blood."

"The word purulent metastasis," says Dance,⁷ "is insufficient to express what occurs in the formation of the lesions consecutive to phlebitis. Before penetrating the organs, the pus mingles first with the blood, which it alters in a special manner; from this alteration result equally special inflammations; and the suppurations which then follow are not the result of a transportation of pus in substance as some have thought."

It will be seen that these opinions tend to the speculative idea that the secondary lesions are to be regarded as the special dynamic effects of a peculiar alteration of the blood; an idea which subsequently received its development in the doctrine of a pyæmic dys-

¹ Breschet. De l'inflammation des veines et de la Phlebite. (Jour. Comp. du Dict. des Sci. Méd., t. ii. p. 325, t. iii. p. 317.)

² Velpeau. Recherches et observations sur la Phlegmatia alba dolens. (Arch. Gén., t. vi. p. 220, 1824.)

³ Bouillaud. Recherches clinique pour servir à l'histoire de la Phlebite. (Revue Médicale, 1825, p. 424.)

⁴ Andral. Clinique Médicale, t. iv. p. 667.

⁵ Louis. Observation de Métrite sub-aigue avec inflammation des veines uterines. (Archiv. Gén., t. x. p. 338, 1826.)

⁶ Loc. cit., p. 123.

⁷ Loc. cit., t. xix. p. 180.

crasis taught by Rokitansky in the first edition of his pathological anatomy.¹

Such was still essentially the state of the question at the time of the publication of the work of Sédillot,² whose elaborate volume contains a good *résumé* of the principal labors of his predecessors, with much valuable personal observation and experiment, and may be regarded as the most complete and modern exposition of the doctrine of pus-blood. In this work he endeavors to show that pyæmia is always preceded by suppurative phlebitis; that the presence of pus in the blood can be made the subject of actual observation, and that the symptoms and pathological alterations of pyæmia can be experimentally produced in animals by the injection of pus into the veins. Each of these statements has been attacked by Virchow, who, commencing in 1846, with the study of the obstruction of the pulmonary artery by blood clots, was led thence to the consideration of the general question of clot-formation in the bloodvessels during life, the anatomical history of inflammation of the arteries and veins, and finally the question of the phenomena of pyæmia. Virchow's papers on this subject are republished in his *Collected Essays*,³ and an excellent summary of the opinions to which he was led is to be found in his lectures on *The Cellular Pathology*.⁴

The originality and clearness of his doctrine of thrombi and emboli have drawn too exclusive attention to it. Virchow distinctly recognizes the possibility of a very different class of cases from those in which mere thrombous formation is the chief phenomenon. "To these kinds of metastasis in which definite substances, though not in a palpable form, but in solution, find their way into the mass of the blood, careful attention must at all events be paid when we endeavor to unravel the complex mass of conditions which are comprehended under the term pyæmia. I see at least no other possibility of explaining certain more diffuse processes, which do not present themselves in the form of ordinary circumscribed metastatic deposit. To this class belongs that metastatic pleurisy, which develops itself without any metastatic abscesses in the lungs—that seemingly rheumatic articular affection in which no distinct deposit is found in the joints—that diffuse gangrenous inflammation of the subcutaneous connective tissue which cannot be ac-

¹ A Manual of Pathological Anatomy, by Carl Rokitansky. Sydenham Society's Translation, vol. i. p. 381.

² Sédillot. De l'infection purulente. 1849.

³ Virchow. Gesammelte Abhandlungen. Zweite Ausgabe. Hamm, 1862.

⁴ Die Cellular Pathologie. Zweite Auflage. Berlin, 1859.

counted for unless we suppose a more chemical mode of infection. Here we have, as may be seen in cases of variolous and cadaveric infection, to deal with a transference of corrupted, ichorous juices into the body; and we must admit the existence of a dyscrasia (ichorous infection) in which this ichorous substance, which has made its way into the body, displays its effects in an acute form in the organs which have a special predilection for such matters."¹

The general view presented in this paragraph forms the subject of careful discussion in his essay on Emboli and Infection, and nine carefully described instances are presented in illustration of the group of cases in which, on the one hand, "no primary thrombosis is to be discovered, and, on the other, where the condition of the vessels leading to the metastatic focus is not of such a kind that one can thence conclude a primary obstruction of it."² A careful perusal of the essay referred to will show clearly that Virchow had found the doctrine of embolism inadequate to account for many of the phenomena of pyæmia, and that although he attributed to it the formation of metastatic foci in the majority of cases, he is not to be taxed with that exclusiveness on this point which some have attributed to him.

Virchow's doctrine of embolism may be briefly summed up as follows: The starting-point is coagulated blood, contained in some one or more of the veins. The coagulum once formed fills the vein up to the next branch through which the circulation is going on; so long as this is the condition present, no constitutional harm results, but soon "new masses of coagulum deposit themselves from the blood upon the end of the thrombus, layer after layer, the thrombus is prolonged beyond the mouth of the branch into the trunk in the direction of the current of the blood, shoots out in the form of a thick cylinder farther and farther, and becomes continually longer and longer." "It is these prolonged plugs that constitute the source of real danger." "The stream of blood may detach minute particles, hurry them away with it, and wedge them tightly into the nearest system of arteries or capillaries."³

The part whose nutritive supply is thus cut off undergoes chemical changes, and the metastatic focus is the result. We have to do in such cases "with fragments of coagula in a more or less altered condition, and according as this alteration has assumed this or that

¹ Die Cellular Pathologie, Lecture X.

² Gesammelte Abhandlungen, p. 668.

³ Die Cellular Pathologie, Lecture X.

character, the nature of the processes which arise in consequence of the obstruction may also be very different. If, for example, a gangrenous softening has taken place at the original site of the coagulum, the metastatic deposit will also assume a gangrenous character."

Relying upon the process of embolism to explain most of the phenomena of metastasis, and supplementing this by the doctrine of ichorous infection to account for those cases which embolism fails to interpret, Virchow denies each one of the principal statements of Sédillot. He asserts that suppurative phlebitis, as understood by Hunter, Arnold, Dance, and their followers, has no existence; that the pus-like fluid found in the veins is softened fibrin, and not pus; that pus has not been observed in the blood in cases of pyæmia; and that the experimental injection of pus into the blood is not followed by the constitutional symptoms or anatomical alterations of that disease, unless some complicating circumstance interferes, such as the accidental introduction of coagulated fragments, which might act as emboli.

The question of the existence of a suppurative phlebitis has already been referred to as far as comports with the purposes of this paper. Let us for a moment consider the other two questions. Has pus been observed in the blood in pyæmic cases? Can pyæmic symptoms be produced by injections of pus or other substances into the circulation?

First, has pus been observed in the blood in pyæmic cases? It is quite evident that in attempting to answer this question, we must lay aside the statements of observers who used the naked eye alone, since we have seen that decomposing blood-clots may simulate the appearance of pus. But some excellent microscopical observers also have asserted that they have actually seen pus-corpuscles in great numbers, both in the pus-like fluid in the so-called inflamed veins and in the general torrent of the circulation. Hasse¹ says, for example, in discussing the puriform fluid in the veins, "I have, however, likewise found great numbers of genuine pus-globules in inflamed veins." Gluge,² who in his "Pathological Histology" teaches that it is generally impossible to distinguish the pus corpuscles from other similar cells, gives several instances in which

¹ An Anatomical Description of the Diseases of the Organs of Circulation and Respiration. Sydenham Society's Translation, page 16.

² Atlas of Pathological Histology, by Dr. Gottlieb Gluge. Translated by J. Leidy, M. D., Philadelphia, 1853, p. 54, note.

he states that he observed pus in the blood, and especially in the venous blood. Of such instances he says, "It has already been mentioned that although pus-corpuscles have no absolute distinctive characters, yet they are readily recognized, when they possess several nuclei, from the smoother, indistinctly nucleated lymph corpuscles, in which view I entirely correspond with Dr. Lebert." In one of Gluge's cases he gives a figure of the pus-cells found by him in the crural vein after an amputation.¹ In the text he says: "These pus-corpuscles were about a third smaller than normally, although their nuclei were visible, and they were mixed with a few oil-globules." The figure is stated to be magnified 550 diameters, which is certainly an exaggeration, and the corpuscles represented in it are not sufficiently well drawn to enable a definite opinion of their nature and structure to be formed.

Sédillot claims that the pus-corpuscles have a more granular surface, a more distinct outline, are more opaque, and of larger size than the white blood-corpuscles.

Lebert adds that the pus-corpuscles have a more yellowish tinge and larger nuclei. Stress has also been laid upon the presence in pus-corpuscles of several nuclei.

In answer to these and similar statements, Virchow² shows that although perhaps the pus corpuscles of typical pus are somewhat larger than the white corpuscles of the blood, and have somewhat larger nuclei, yet neither possess invariable characteristics. As to size, not only are pus-corpuscles frequently met with quite as small as the smallest white blood-corpuscles, and the latter quite as large as the largest in pus, but abscesses may be met with in which the mass of the corpuscles are larger or smaller than usual, and the same variation in size is true of the white blood-corpuscles. As for a more granular or yellowish appearance or sharper outlines in the pus-corpuscles, these may or may not be present; and, in fact, the appearances of both sets of corpuscles vary greatly with the variations in the composition of the fluid in which they float. Virchow quotes from Becquerel and Rodier³ to show that even in puerperal fever and anæmia, the blood contains less water than is usually present in pus. He argues that the blood serum is usually denser than the pus serum, and accounts in this way for the usually smaller size of the white corpuscles. He hence concludes that the

¹ Loc. cit., Plate I., fig. 12.

² *Gesammelte Abhandlungen*, p. 646.

³ *Traité de Chim. Path.*, pp. 122, 154, 570.

diagnosis of pus in the blood is difficult, if not impossible, and shows that those cases in which the whole blood has appeared under the microscope to be mixed with pus, are really cases of leukæmia, the corpuscles being in fact white blood-corpuscles in abnormally increased numbers. My own observations have satisfied me that in the main these statements are quite correct. I have frequently observed and measured white blood-corpuscles, mucous corpuscles from the mouth, vagina, and mucous surfaces, and pus-corpuscles, collected under the most varied circumstances, and have not been able to satisfy myself that a single constant peculiarity exists by which a diagnosis can be made. All these bodies when recently formed are spherical granular cells, which may vary considerably in size, and which contain most frequently from one to four nucleus-like bodies also of variable size. Perhaps the average diameter of the pus and mucous corpuscles is slightly greater than that of the white blood-corpuscles; but pus is frequently to be met with containing corpuscles no larger than those of the blood, and not only are individual corpuscles as large as any in pus often to be met with in the blood, but sometimes great numbers of them are present, especially in the blood of leukæmic patients.

Perhaps it is true that corpuscles, with single nuclei, are more frequent in the blood and mucus, those with several in pus; but the reverse occasionally takes place, and I have seldom examined a sample of either of the liquids without finding specimens of each kind. In March, 1866, I compared carefully the white corpuscles of my own blood, with the mucous corpuscles of my saliva, and the corpuscles of a drop of pus from a small alveolar abscess with which I was at that time annoyed. The majority of the white blood-corpuscles observed, measured eight or nine thousandths of a millimetre; a number were as large as ten, and a few eleven. The majority of the pus-corpuscles were nine to ten, many of them reaching eleven, and a few twelve. The majority of the mucous corpuscles measured ten to nearly eleven. On the addition of acetic acid, the majority of the cells in all the fluids were found to contain from one to four nuclei. But it happened that the double and triple nuclei were most numerous in the blood and least so in the pus. Next day most of the pus-cells from the same abscess contained double and triple nuclei.

On the whole, therefore, it may be concluded that the diagnosis of blood, pus, and mucous corpuscles, is to be founded in any case

on the situation in which the corpuscles are found, the nature of the fluid in which they float, and the careful consideration of all the circumstances of the case, rather than upon the size or character of the corpuscles themselves.

Secondly, can pyæmic symptoms be produced by injections of pus or other substances into the circulation? From a very early period in the history of the discussion, attempts were made to produce metastatic foci, and the symptoms of putrid infection, by artificial means; and the introduction chiefly in the veins, but sometimes also into the arteries, of various solid substances, of pus, and of putrid liquors of different kinds, has been experimented on by a number of observers with variable results.

Gaspard and Cruveilhier injected quicksilver into the veins, and produced thus tubercle like foci in the lungs, some of which contained globules of mercury in their centres. This experiment was subsequently repeated by various persons, among others, by Virchow, who failed to obtain the tubercle-like foci. Still later the matter has been investigated by Panum,¹ who obtained results opposed to Virchow, and similar to those of Cruveilhier. Panum explains that Virchow killed his animals within forty-eight hours after injecting the mercury, while Cruveilhier and himself waited usually several days to give time for the foci to form. Cruveilhier attributed the results observed in his experiments simply to obstruction of a branch of the pulmonary artery. But Virchow showed that, like obstructions produced by the introduction of pieces of India-rubber into the jugular vein, which were carried into the circulation, to be impacted in the small pulmonary arteries, created no similar local irritation, and Panum found that little balls of wax, similarly introduced, simply become encysted. Panum hence concludes with reason that the mercury globules, once fixed, act in some way as an irritant to the surrounding lung tissue, and not merely as a mechanical obstruction.

More positive results were obtained by the injection of organic liquids in a state of septic alteration. After such injections, Gaspard² obtained gangrenous foci in the lungs. Trousseau and Dupuy injected into the veins of two horses a putrefying liquid obtained by the maceration of flesh. Grave constitutional disturbances were produced in both cases; in one, red foci were found in the lungs;

¹ Experimentelle Beiträge zur Lehre von der Emboli. Prof. Dr. P. L. Panum in Kiel. (Virchow's Archiv, Band xxv. s. 449; 1862.)

² Journ. de Phys., par Magendie, 1822, t. ii. p. 1; 1824, t. iv. p. 1.

in the other, petechia and ecchymoses in all the organs of the body.¹ Nearly similar results were obtained by Leuret, by the transfusion of the blood of a horse affected by charbon into a healthy mare.² Sédillot also gives a number of cases in which he obtained well-marked gangrenous foci in the lungs after putrid injections. On the other hand, Castelnau and Ducrest asserted that putrid injections prove fatal without leading to the formation of abscesses, and Stich³ explains the results of Sédillot by supposing his experiments to have been made without sufficient precautions against small solid fragments which might act as an emboli. Panum agrees with Stich in his opinion that metastatic foci will not be formed after putrid injections, if the fluid injected is carefully filtered. He quotes several experiments of his own in proof of this opinion. In these the fluid injected was obtained by letting dog's flesh putrefy in distilled water, and afterward filtering it. He obtained, however, metastatic foci, and the general symptoms of pyæmia, by introducing into the veins solid fragments in a state of decomposition or thoroughly soaked in the putrid fluid.

Virchow obtained in the main similar results, but, more moderate than Stich and Panum, does not hold the experiments hitherto performed quite conclusive. On the one hand, he objects that most of them have been performed either on dogs, which are extremely resistant to putrid and purulent affections, or on rabbits, which perish under comparatively trifling lesions, and so give little opportunity for prolonged experiment; on the other hand, he calls attention to the fact too generally overlooked that the products of putrefaction depend so closely upon the temperature and other circumstances under which it occurs, that the fluid obtained by letting flesh putrefy in water in the open air at ordinary temperatures, is scarcely to be regarded as the equivalent of any of the products of the putrefactions or decompositions which actually go on within the human body in diseased conditions. He therefore regards the question as one which demands further investigation before a satisfactory conclusion can be reached.

Like contradictions exist in the statements of experimenters with regard to the effects of injections of *pus* into the blood, on which

¹ Trousseau and Dupuy. Expériences et observations sur les altérations du sang considérées comme causes ou comme complications des maladies locales. Archiv. Générales, t. xi. p. 373, 1826.

² Leuret. Recherches et expériences sur l'altération du Sang. Archiv. Générales, t. xi. p. 98, 1826.

³ Stich. Annalen des Charité-Krankenhauses, iii. s. 192, 1852.

indeed the experimental proof of the doctrine of pyæmia depends. Dupuytren¹ failed to produce metastatic abscesses by the injection of pus into the veins. Trousseau and Dupuy, by repeated injections of pus into the veins of a horse, obtained constitutional disorder and the production of a peculiar inflammation of the subcutaneous cellular tissue of the thorax. Gunther² failed to produce any anatomical alteration by the injection of healthy pus. The same failure attended Sédillot in many single injections of pus. Castelnau and Ducrest³ attempted to imitate the conditions supposed to occur in purulent phlebitis more closely by repeating the injections so that a constant purulent supply might be maintained. Under these circumstances, they succeeded in developing metastatic foci. Similar success attended Sédillot and more lately Gamgée⁴ and Lebert.⁵

On the other hand, Beck⁶ attributes all successes of this kind to a want of due precaution on the part of the experimenters, which permitted the introduction of solid or semi-solid fragments capable of acting as emboli, and gives fourteen cases of pus injections by himself in which no abscesses were produced. Virchow takes essentially similar grounds; he points out that Sédillot, by leaving the canula tied in the vein for several days, for the purpose of facilitating repeated pus injections, greatly favored the probability of the accidental introduction of small coagula or other fragments, and arrives at the following conclusions as the results of his experiments: First, the injection of undecomposed, normal, non-specific pus into the veins, if performed with proper precautions, produces generally no considerable anatomical alteration, and especially no metastasis even when the injection is frequently repeated in the same animal. Secondly, the careless injection of unfiltered or very coherent pus, especially when frequently repeated through the same vein, produces manifold foci of inflammation and suppuration. Thirdly, if putrid or specific pus is used, the foci assume a putrid or specific character. Fourthly, injections into the arteries give similar results.

We have finally to mention the experiments of Virchow and

¹ See Sédillot, p. 66.

² Rust's Magazin, Band xxx. s. 332, 1834.

³ Mém. de l'Acad. de Méd. 1846, t. xii.

⁴ Gazette Méd. de Lyon, 1855.

⁵ Krankheiten der Blut- und Lymph-Gefässe, by H. Lebert, in Virchow's Handbuch der Speciellen Pathologie und Therapie, t. v. p. 90.

⁶ Unters. u. Studien im Gebiete der Anat. Phys. u. Chir. s. 45, 1852.

Panum on the introduction of artificial emboli into the veins. Virchow placed in the jugular vein of dogs, fibrin clots from various sources, coagulated blood from human thrombi, and small fragments of muscle; violent pneumonic affections, with pus-formation or necrosis of parts of the lung tissue, and other disturbances followed these experiments.

Panum's paper, already quoted, also contains an ingenious series of experiments. Having shown that small wax balls introduced into the jugular vein become merely encapsuled in the lungs, like Virchow's fragments of India rubber, but did not produce abscesses; that the injection of the putrid liquid from meat, if carefully filtered, killed, but produced no secondary foci; even if wax balls were simultaneously introduced to obstruct the pulmonary vessels; he adduces two series of observations, in one of which solid animal substances, in a state of decomposition, or infiltrated with putrid fluid, in the other quite fresh coagula of healthy blood were introduced into the veins. In the first class of cases foci of inflammation and suppuration were uniformly found in the lungs. The same occasionally occurred in the second series, but generally no considerable alteration of the lung tissue was noticed, except minute fibroid points resembling miliary tubercle, the precise nature and origin of which are not clearly made out. Panum had previously published a paper on transfusion of blood,¹ in which he lays great stress on the dangers of transfusion unless performed with defibrinated and carefully strained blood. Further experiments on the consequences of the introduction of the fresh blood coagula are necessary, however, to explain the irregularity of these results.

In concluding this sketch of the general pathology of pyæmia, I may be permitted to state briefly how far the views hitherto sketched, and especially those of Panum and Virchow, correspond with my own personal observations. And first I must freely admit that careful examination of the secondary foci has usually failed to show me emboli impacted in the arterial twig, by which the region of the focus is supplied. On the contrary, the vessel continues generally quite patulous even after it is involved in the substance of the morbid nodule. This I have observed in a case of foci in the lungs consecutive to syphilitic suppuration of the tibia, as well as in a number of similar cases due to wounds and amputations. I have investigated the branches of the portal vein leading into similar

¹ Exper. Unter. über die Transfusion. (Virchow's Arch. Band xxvii. s. 240, 433.)

foci in the liver in cases of ulcerative dysentery with like results. On the other hand, how frequently has it occurred to me to see the most diverse coagula in the veins leading from an amputated limb where death has occurred from other causes, without any pyæmic symptoms, and where the most critical examination of the body has failed to discover any secondary foci.

Next, I may mention that so far as my own personal observation has gone, the pyæmic phenomena have been invariably connected with the primary occurrence of local septic processes. I do not mean to lay this down as an unchangeable law. My observations have not been as yet sufficiently numerous to make me positive of more than that this is at least an important and frequent group of cases. In cases of wounds the local conditions brought under my notice were chiefly sloughing of the edges of the wound, and the peculiar gangrene of the marrow which has so generally been mis-called osteo-myelitis. This latter word has played so conspicuous a role that it is impossible to pass it by without notice. That there is an osteo-myelitis—a true inflammation of the marrow—is beyond a doubt. It gives rise to the changes which accompany the rounding of the bone after amputations; it is connected with the reparative effort after fractures; in unfavorable cases it terminates in supuration. When it spreads along the bone the affected marrow becomes reddened, often indurated, occasionally a series of discrete abscesses forms; occasionally the whole marrow is bathed in pus. But this condition, to which alone the term osteo-myelitis properly belongs, is usually unaccompanied by formidable constitutional disturbances, and is very generally overlooked entirely by the practitioner. The peculiar gangrene of the marrow which in armies and great general hospitals plays so formidable a part, may set in before any true inflammation has occurred in the marrow, or at any stage whatever of the inflammatory process, and taking its origin in the sloughing flaps or edges of the wound may involve the inflamed portion of the marrow, and thence spread rapidly beyond along the healthy marrow which it speedily reduces to a greenish-yellow or brownish-green stinking pulp. This condition I have seen extend to the head of the femur after amputations at the lower third; I have known it to spread throughout the whole length of the femur in cases of contusion of the bone by balls without fracture.

Where death has taken place before the whole marrow has been involved, the region of transition between the healthy marrow and the gangrenous part affords the opportunity for studying the steps

of the process. The gangrene is not preceded by redness, by effusion, by cell multiplication, by anything that can be construed into inflammation. The first phenomenon noted is the peculiar coagulation of the blood in the bloodvessels, and the granular aspect of the tissues under the microscope, which shows that the part is already dead, and that decomposition has commenced. The subsequent changes are purely chemical, and the normal elements become less and less recognizable amidst the host of actively moving molecules set free by the putrefactive alteration. The process is in fact only to be compared with the most destructive and rapidly progressing form of gangrene of the external soft parts. Energetic as it is, however, it does not always prove fatal, especially in the cases which follow amputations. A line of demarcation may be formed by a true inflammatory process, and the dead tissue may separate as a slough, the prominent part of which is a cylindrical tube of bone of variable size, representing usually the whole shaft at the point divided by the saw, and from the eighth of an inch to an inch above it; thence an irregularly eroded cylinder of variable length. I have seen these tubes seven or eight inches long.

But in the cases which prove fatal by inducing pyæmia, no line of demarcation, no barrier of inflammation limits the gangrenous portion, and the veins leading from the affected bone are usually full of coagula which have entered into a form of putrefaction quite similar to that going on in the marrow. The ultimate result of this change is a yellowish or greenish-yellow fetid fluid, in which the microscope recognizes nothing but actively moving molecules with bright centres and dark borders. I have once or twice seen the veins leading from the flaps of a sloughing stump in a similar condition, but in most of the cases to which my attention was drawn the veins affected proceeded directly from the diseased bone itself. The putrefactive change going on in the marrow is transmitted through the coagulated blood mass in the veins by actual continuity. The femoral vein, the saphena and their branches were sometimes stuffed with thrombi throughout a part of their extent, but in all the cases I found the veins from the bone, filled with their fetid contents, were clearly traceable to the point where the trunk with which they were connected discharged into the femoral, or one of the larger branches with no thrombi intervening on the cardiac side. The granular yellowish fluid could sometimes be traced some little distance towards the heart. In short, there was clear anatomical proof of the introduction into the torrent of the circulation of the

putrefying debris of the coagula which had formed in the veins leading from the affected bone.

As for the detaching of larger fragments which should deserve the name of emboli, I found no actual anatomical proof, though abundant possibility for such an occurrence existed. What was to be seen discharging into the femoral vein was simply the putrefying liquid described, a liquid more viscid than blood, which could not be expected to circulate as readily as blood, which might readily, I admit it, although I saw nothing of the sort, carry with it more coherent fragments of the involved coagulum, but which, in any case, might be expected to be arrested in the capillaries of the lungs, and if so arrested, to set up there, by actual contact, a similar form of change. It is also easier to conceive how a part of such a viscid, putrid fluid, which had passed through the capillaries of the lungs, might subsequently be arrested in the systemic capillaries, than it is to account for the frequent occurrence of foci in the liver and kidneys after amputations of the thigh on the supposition of solid emboli.

I do not offer this summary of my own observations as a solution of the question of pyæmia; rather as a statement of facts, difficult to account for on the supposition of emboli, impossible to account for on the supposition of suppurative phlebitis, which must yet be fully embraced by any satisfactory explanation of the disease. The general series of phenomena here sketched, as observed in connection with wounds, perfectly accords with what I have been able to observe in puerperal pyæmia, and in the pyæmia connected with dysentery. In the inflamed womb of the first group of cases, and the colon ulcers of the second, all the autopsies I have witnessed or made, demonstrated the existence of gangrenous or phagedenic, that is, septic processes in connection with the local lesion. Without insisting upon any exclusiveness for the opinions which must necessarily spring from such cases, it is difficult to avoid the conclusion that local septic processes have a significant connection with the genesis of pyæmia, and that viscid septic liquids derived from the degenerating primary coagulum may at times play the part which Virchow ascribes only to solid emboli.

These considerations assume still more importance when an attempt is made to arrive at some definite notion with regard to the *causes of pyæmia*. Truly it must be admitted that our knowledge of these causes is yet more unsatisfactory than our knowledge of the pathology of the disease. It is well known, however, that the

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conditions under which it most certainly develops itself are those under which almost all zymotic diseases attain their greatest malignancy; and it will readily be understood, if the views I have hinted are correct, that whatever favors the occurrence of septic processes in the local lesion may become a cause of pyæmia. Hence it is in crowded hospitals, where ventilation, cleanliness, and diet are comparatively neglected, and among patients debilitated and disordered by previous exposures and privations that pyæmia secures most victims, whether among wounded soldiers or parturient women. Under the same circumstances, erysipelas, hospital gangrene, and sloughing of wounds and sores become common, very often indeed appear to stand in direct genetic connection to the subsequent pyæmia. Whether besides such hygienic conditions, to which in modern times attention has been most exclusively directed, there lurk yet other and more obscure momenta; whether above all, as has been especially claimed by the obstetricians, there is a peculiar, pyæmic, epidemic influence which exists at certain times and places, and is absent at others, is a question which can be first intelligently approached when an epidemic of pyæmia shall have been observed under circumstances which completely fulfil every well-known hygienic requirement: until then to insist upon this aspect of the question tends to encourage and excuse the neglect of conditions whose influence is beyond question.

After the foregoing remarks on the general relations of pyæmia, it remains to consider briefly its more important varieties. Passing by the strictly surgical relation of the subject, I shall first speak of *puerperal pyæmia*. Puerperal pyæmia embraces the group of cases which occur in parturient women in connection with the local changes which have been most generally described under the name of uterine phlebitis. The disease constitutes one of the most formidable types of the so-called puerperal fever. The general symptoms during life do not differ from those of pyæmia as already described, and after death the metastatic foci often found, especially in the liver and lungs, and the state of the veins leading from the uterus, particularly those connected with its placental region, differ in no essential particular from what is seen in pyæmia consecutive upon wounds. The condition of the womb itself in these cases requires a more exact anatomical investigation than appears as yet to have been bestowed upon it. It is generally spoken of as inflamed; often abscesses are said to exist in the substances of its

walls. In the cases which have been brought within my own personal investigation, I have found no satisfactory anatomical proof, either of inflammation or abscesses. On the contrary, what was to be observed in the general tissue of the womb itself was merely the usual retrograde metamorphosis (fatty degeneration of the muscular tissue) which follows parturition. A putrid condition of the inner surface of the organ, however, existed, extending to a variable depth, and coagula filled the uterine veins, especially those corresponding with the placental surface. Septic metamorphosis existed in these precisely as in the similar coagula in the veins leading from bones affected with gangrene of the marrow.

In the earlier periods of medical literature the cases now under consideration were confounded under the general designation of puerperal fever, but immediately after the essay of Hunter on phlebitis, the English obstetricians began to discriminate a class of cases which they supposed to be best described under the name of uterine phlebitis. Clarke¹ found what he considered to be pus in the uterine veins of a woman who had died after labor, and Wilson² described the morbid appearance of one case, and alluded to others in which inflammation of the uterine veins had existed and even extended to the cava. Both Arnott and Dance drew from uterine pyæmia the most important of their illustrative cases, and subsequently there are few writers on phlebitis and pyæmia who fail to refer to the puerperal form. Virchow, in his "Cellular Pathology" (Lecture X.), appeals to the facts observed in an epidemic of puerperal fever in Berlin to support his doctrine of emboli, and H. Meckel³ and Kiwisch⁴ in the main adopt his views of the part played by thrombi and emboli in the production of the secondary lesions.

It is not very easy to separate the consideration of puerperal pyæmia from that of *phlegmusia dolens*; an affection of the lower extremities, which, although chiefly met with in the parturient female, is not always confined to this condition or indeed to the female sex. It is characterized by the development of a peculiar œdema, the affected limb becoming painful to the touch, with swell-

¹ Practical Essays on the Management of Pregnancy. London, 1793, p. 70.

² Transactions of a Society for the Improvement of Medical and Chirurgical Knowledge, vol. iii. p. 65.

³ H. Meckel, Annalen des Charité-Krankenhauses, v. s. 276.

⁴ Kiwisch, Klinische Vorträge über spec. Pathologie u. Therapie der Krankh. des weiblichen Geschlechtes, 1851, Band I., s. 630.

ing and induration in the course of the veins. It may affect one limb or both; in the latter case either successively or simultaneously. It may produce comparatively little constitutional disturbance, or may be accompanied by the usual symptoms of pyæmia with a fatal result. In the latter case, degenerating coagula in the uterine as well as the crural veins, pelvic abscesses, abscesses in the femoral subcutaneous tissue, and secondary foci of the viscera are the conditions most frequently observed. Bouillaud¹ was among the first to connect this peculiar swelling with obstruction of the veins, and Dr. Davis, in the same year published an able paper in which he makes the attempt to connect the condition with phlebitis of the crural veins.² According to Dr. Davis four different theories had previously been propounded; that of Mauriceau³ that it was due to a reflex "of humors which ought to be evacuated by the lochia;" that of Puzos⁴ "that it was due to the metastasis of milk," which was also adopted by Levret;⁵ that of White and Trye, that it was due to obstruction or other morbid states of the lymphatics, and that advocated by Dr. Hull in his essay on phlegmasia dolens, published in 1800, that it "consists in an inflammatory affection, producing suddenly a considerable effusion of serum and coagulable lymph from the exhalants into the cellular membrane of the limb." The next year Velpeau published a paper on the same subject, in which he arrived at essentially the same conclusions as Davis had done.⁶ And still further development was given to the idea by the labors of Dr. Robert Lee,⁷ who particularly insisted upon the extension of inflammation from the uterine veins to the crural as explaining the origin of the affection. On the other hand, Mackenzie⁸ dis-

¹ De l'obliteration des veines, etc. M. Bouillaud. (Archiv. Gén., t. ii. p. 188. 1823.)

² An Essay on the Proximate Cause of the Disease called Phlegmasia Dolens, by David D. Davis, M. D. (Medico-Chirurg. Trans., vol. xii. p. 419. 1823.)

³ Traité des Maladies des Femmes Grosses et de celles qui sont accouchées, 5me edit., t. i. p. 446.

⁴ Puzos. Mémoire sur les depot laiteux.

⁵ Levret. L'art des accouchements.

⁶ Recherches et observations sur la Phlegmatia alba Dolens. M. Velpeau. (Archiv. Gén., t. vi. p. 220. 1824.)

⁷ Robert Lee. A Contribution to the Pathology of Phlegmasia Dolens. (Med. Chir. Trans., vol. xv. p. 132. 1829.) Pathological Researches on Inflammation of the Veins of the Uterus, with Additional Observations on Phlegmasia Dolens. (Ib., vol. xv. p. 369.) Further Researches on Phlegmasia Dolens. (Ib., vol. xxxvi. p. 281. 1853.)

⁸ Researches on the Pathology of Obstructive Phlebitis and the Nature and

puted the general correctness of the popular doctrine of phlebitis, and especially its application to the interpretation of phlegmasia dolens, which he regarded as due to non-inflammatory clot formation; a view also adopted by Virchow in his account of this affection. Of course, the ultimate interpretation of phlegmasia dolens will be determined by the prevalent doctrines on phlebitis, thrombosis, and infection; at present, however, the uniform existence of thrombi in these cases, and the comparative rarity of pyæmic symptoms may be particularly mentioned as of doctrinal importance. According to Mackenzie, of sixty cases of puerperal phlegmasia dolens only twenty proved fatal.

The *pyæmia of new-born children* connected with erysipelatous and gangrenous conditions of the naval, which is generally described under the head of phlebitis of the umbilical vein, may next be briefly mentioned. Described early in the present century by Breschet, Duplay, and Trousseau, this affection has comparatively recently been carefully studied by H. Meckel¹ in La Charité at Berlin. The affection is seldom observed except in hospitals and among the squalid children of the poor. It begins as a suppurative, erysipelatous or gangrenous affection of the navel, followed by thrombus formation in the umbilical vein, occasionally in the portal vein; secondary foci in the liver, lungs, etc., result. According to H. Meckel, abscesses in the lungs and subcutaneous tissue occasionally occur without foci in the liver. Peritonitis often accompanies the disease, and jaundice and diarrhoea are frequent symptoms. The course of the affection does not differ from other cases of pyæmia. It almost always terminates fatally.

Of more general significance to the medical practitioner than any group of pyæmic cases, except those connected with the puerperal state, are *those which spring from ulceration of the bowels* and other conditions connected with the parts whose venous branches terminate in the portal vein. These cases have been the subject of numerous essays and studies, and after the memoir of Franconneau Dufresne,² and the publication of Lambron's³ remarkable case

Proximate Cause of Phlegmasia Dolens. F. W. Mackenzie, M. D. (Med.-Chirg. Trans., vol. xxxvi. p. 169. 1853.)

¹ H. Meckel. Ueber die Entzündung des Nablevenen. Annalen der Charité, 1854.

² De l'inflammation du système veineux abdominal, par le Docteur Franconneau Dufresne. (Gazette Médicale de Paris du 16 Novembre, 1839.)

³ Observations d'inflammation de veins du foie, par Ernest Lambron. (Archiv. Gén. 3me serie, t. xiv. p. 129. 1842.)

in which a fish bone swallowed by an old man found its way through the walls of the stomach, transfixing the portal vein, and gave rise to a fatal pylephlebitis, numerous cases and remarks on pylephlebitis were published by different observers, among others by Frey, of Manheim,¹ Waller,² and Oppolzer,³ of Prague, and Hennoch,⁴ of Berlin. The excellent paper of Leudet⁵ may also be mentioned. All these, and most of the subsequent essays, including the section on inflammation of the portal veins in Budd's work on the liver,⁶ describe phlebitis of the portal vein as consisting of two varieties, the adhesive and the suppurative, and in the details of the local description agree with the general account of phlebitis as received by their contemporaries. More modern views are expressed in the treatise on diseases of the liver by Frerichs,⁷ who, while still speaking of adhesive and suppurative pylephlebitis, clearly recognizes the frequency of thrombus formation in the portal vein without inflammation, and especially in his description of suppurative pylephlebitis, shows his understanding of that process to be much more in accord with modern doctrines than the names he still employs would indicate. "The thrombus in the interior of the vein undergoes destruction at an early period. It softens from the centre into a dirty greenish-red pulp, and afterwards dissolves more or less completely into a purulent fluid." "Not unfrequently metastatic deposits are developed, as in other forms of phlebitis, by particles of thrombi being floated by the blood into the liver; these deposits are found in various stages of development, from reddish-brown infarctions to yellow cavities of pus."⁸

The affection usually described under the name of pylephlebitis, is characterized by abdominal pain, usually in the epigastrium or right hypochondriac region, with rigors, fever, enlargement of the liver and spleen, followed by jaundice, symptoms of diffuse peritonitis, delirium, and a fatal typhoid condition with or without evi-

¹ Heidelb. Annal., t. x. 1844, in Archiv. Gén., 4me serie, t. vii. p. 483.

² Wiener Zeitung, 1846, in Archiv. Gén., 4me serie, t. xviii. p. 462.

³ Prager Vierteljahrsschrift, t. i. p. 110. 1849.

⁴ Klinik der Unterleibs-Krankh., p. 188. Berlin, 1852.

⁵ Recherches sur la Phlebite de la veine porte. (Archiv. Gén., 5me serie, t. i. p. 145.)

⁶ On Diseases of the Liver. By George Budd, M. D. 3d ed. London, 1857, p. 170.

⁷ A Clinical Treatise on Diseases of the Liver. By Dr. F. T. Frerichs. Edit. of New Sydenham Society, London, 1861.

⁸ Loc. cit., vol. ii. p. 408.

dence of metastatic foci in the lungs and joints. It usually runs its course in from four to six weeks, but may prove fatal earlier, or may be protracted longer. It may be due to ulcerations of the alimentary tract, abscesses of the spleen or mesenteric glands, disturbances due to gall-stones, etc. Here, as elsewhere, it is necessary, however, to distinguish between mere thrombus formation and those cases which terminate in pyæmia. In the cases which result from chronic dysenteric ulcers of the colon, the patient, after having suffered from dysentery for a variable period, suffers a chill, or a series of chills, followed by the usual constitutional symptoms of pyæmia with fatal issue. After death metastatic foci in various stages of development are found in the liver, the lungs, the spleen, or elsewhere. A similar form of pyæmia occurs in connection with typhoid ulcers of the small intestines.

Intimately allied to the question of pyæmia originating in dysentery, is the special subject of abscess of the liver occurring in that disease. Budd, in his treatise on the liver, attributes all abscesses of this organ, except those resulting directly from blows or injuries, to "suppurative inflammation of some vein, and the consequent contamination of the blood by pus." Bristow¹ attacked the exclusiveness of this explanation, speaks of tubercular abscesses, abscesses due to hydatids, to obstruction of the hepatic ducts by gall-stones, etc., but admits the occasional applicability of Budd's views, and regards the hepatic abscess of dysentery as due to phlebitis of the mesenteric veins. Frerichs² enumerates as causes contusions or other traumatic agencies, metastatic or pyæmic inflammation of the liver, inflammatory and ulcerative processes in the gastro-intestinal canal, and inflammation and ulceration of the bile ducts. The whole matter possesses great interest, but at present I must be content with this passing notice.

Besides the foregoing more important varieties, pyæmia may result from a great number of other morbid conditions, among others from syphilitic or other diseases of the bones, and from rheumatism, as in the cases of Habershon³ and Bennett.⁴ Haber-

¹ On the Connection between Abscesses of the Liver and Gastro-Intestinal Ulceration. (Trans. of Path. Society of London, vol. ix. p. 241, 1858.) On the Modes in which Hepatic Abscesses may be formed, etc. (Ib., p. 273.)

² Loc. cit., vol. ii. p. 110.

³ Guy's Hospital Reports, 1859.

⁴ Clinical Lectures, Am. ed., 1860, p. 847.

shon, indeed, goes so far as to suggest that gonorrhœal rheumatism is generally a form of pyæmia.

Finally, we have to consider the so called *idiopathic* or *spontaneous pyæmia* of the Vienna school,¹ to which attention has recently been drawn by Wunderlich. Wunderlich² indicates by the idiopathic pyæmia simply those cases in which the cause is hidden and cannot be traced to the local lesion in which it originated. But this moderate view has not always prevailed. I will not attempt to trace the full history of the confused statements that have been made. It is sufficient to state that a pyæmia which is without typhoid symptoms, and without secondary foci—which is predicated wholly upon the presence in the blood of bodies believed from their microscopical appearances to be pus-corpuscles, is not pyæmia, but leukæmia, or white blood. The existence of true cases of pyæmia for which no local cause can be found cannot, however, be denied, though their appearance is comparatively rare. Cases which take their origin in idiopathic erysipelas or gangrene are much more frequent, and are properly embraced in the notion of spontaneous pyæmia. Among these latter cases there is an interesting form in which metastatic foci occur in the skin. Dance gives two cases of this sort; the first,³ a true case of spontaneous pyæmia; the second, originating in idiopathic gangrene of the right little finger. In both the history of pyæmia was undoubted, and metastatic foci were found in the lungs as well as in the skin. I have myself had my attention drawn to a similar case taking its origin in idiopathic erysipelas.

In concluding this paper, I have to express my regret that other engagements have not permitted me to bestow upon the subject the time and labor it so well deserves. But a detailed criticism of its literature, with an attempt to throw further light on the open questions by experimental researches, would occupy a volume, and I have been compelled to content myself with this brief survey of the present state of our knowledge, which I trust may not be found devoid of interest.

¹ Rokitansky, Path. Anat. Sydenham Soc. Edit., vol. i.

² Wunderlich, from Archiv. für Phys. Heilkunde, in Gazette Médicale de Paris vol. xxx. p. 422. 1858.

³ Loc. cit. Archiv. Gén., t. xii. p. 30.

that, indeed, there is no doubt that pyemic phenomena
is generally a form of pyemia.
It is for the sake of making the so-called pyemic or pyemia-
ous cases of the Vienna series, the pyemic cases, has recently
been shown by Weiskopf. Weiskopf's evidence by the blood
this pyemia simply shows cases in which the cause is hidden and
cannot be traced to the local lesion in which it originated. That
this is the case has been already proved. I will not attempt
to trace the path of the pyemic process, but have only
to indicate that it is difficult to state that pyemia is a
pyemic pyemia, and a local pyemia, which is pyemic
and which is the pyemia in the blood of bodies believed
to be pyemic, pyemic pyemia, to be pyemic pyemia, is not
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ever, for which the local cause can be found, cannot be
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1. Weiskopf, *Ueber die Pyämie*, Leipzig, 1871.
2. Weiskopf, *Ueber die Pyämie*, Leipzig, 1871.
3. Weiskopf, *Ueber die Pyämie*, Leipzig, 1871.
4. Weiskopf, *Ueber die Pyämie*, Leipzig, 1871.